

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No.: **ISPH-0763**

Inventors: **Monia et al.**

Serial No.: **Not Yet Assigned**

Filing Date: **Herewith**

Examiner: **Not Yet Assigned**

Group Art Unit: **Not Yet Assigned**

Title: **Antisense Oligonucleotide Inhibition of RAS**

"Express Mail" Label No. **EL976562867US**

Date of Deposit **August 18, 2003**

I hereby certify that this paper is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Commissioner for Patents, Mail Stop Sequence, P. O. Box 1450, Alexandria, VA 22313-1450.

By Jane Massey  
Typed Name: **Jane Massey Licata, Reg. No. 32,257**

Commissioner for Patents  
Mail Stop Sequence  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

**INFORMATION DISCLOSURE STATEMENT**

Pursuant to 37 C.F.R. §1.56 and in accordance with 37 C.F.R. §§1.97-1.98, information relating to the above-identified application is hereby disclosed. Inclusion of information in this statement is not to be construed as an admission that this information is material as that term is defined in 37 C.F.R. §1.56(b).

(XX) In accordance with §1.97(b), since this Information Disclosure Statement is being filed either within three months of the filing date of the above-identified application, within three months of the date of entry into the national stage of the above identified application as set forth in §1.491, or before the mailing date of a first Office Action on the merits of the above-identified application, no additional fee is required.

( ) In accordance with §1.97(c), this Information Disclosure Statement is being filed after the period set forth in §1.97(b) above but before the mailing date of either a Final Action under §1.113 or a Notice of Allowance under §1.311, therefore:

( ) Certification in Accordance with §1.97(e) is set forth below; or

( ) The fee of \$180.00 as set forth in §1.17(p) is attached.

( ) In accordance with §1.97(d), this Information Disclosure Statement is being filed after the mailing date of either a Final Action under §1.113 or a Notice of Allowance under §1.311 but before the payment of the Issue Fee, therefore included are: Certification in Accordance with §1.97(e); Petition Requesting Consideration of the Information Disclosure Statement; and the fee of \$130.00 as set forth in §1.17(I)(1).

( ) Copies of each of the references listed on the attached Form PTO-1449 (modified) are enclosed herewith.

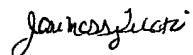
(XX) In accordance with §1.98(d), copies of some or all of the references listed on the attached Form PTO-1449 (modified) are not enclosed herewith because they were previously submitted to the U.S. Patent and Trademark Office in prior application Serial No. 09/870,002, filed May 30, 2001, 09/575,554, filed May 22, 2000, Serial No. 09/128,494, filed August 3, 1998, Serial No. 08/889,296, filed July 8, 1997, Serial No. 08/411,734, filed April 3, 1995, Serial No. 08/007,996, filed January 21, 1993, or Serial No. 07/958,134, filed October 5, 1992 for which a claim for priority under 35 U.S.C. §120 has been made in the instant application.

Please charge any deficiency or credit any overpayment to Deposit Account No. 50-1619. This form is submitted in duplicate.

( ) The relevance of the listed references in a foreign language is as stated in the specification at pages @@.

(XX) All listed references are in the English language.

Respectfully submitted,



Jane Massey Licata  
Registration No. 32,257

Date: August 18, 2003

Licata & Tyrrell P.C.  
66 E. Main Street  
Marlton, New Jersey 08053  
(856) 810-1515

Form PTO-1449 Modified		Docket No. ISPH-0763	Serial No. Not yet assigned
List of Patents and Publications Cited by Applicant (Use several sheets if necessary)		Applicant Monia et al.	
U.S. Department of Commerce		Filing Date herewith	Group Not yet assigned

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	AA	Anfossi et al., "An Oligomer Complementary to c-myb-encoded mRNA inhibits proliferation of human myeloid leukemia cell lines", <i>Proc. Natl. Acad. Sci.</i> 1989, 86, 3379-3383
	AB	Borer, P.N., Dengler, B., Tinoco, I., Jr., and Uhlenbeck, O.C., "Stability of Ribonucleic acid Double-stranded Helices", <i>J. Mol. Biol.</i> , 1974, 86, 843-853
	AC	Brown et al., "Modulation of ras Expression by Anti-sense, Nonionic Deoxyoligonucleotide Analogs", <i>Oncogene Research</i> 1989, 4, 243-252
	AD	Capon et al., "Complete nucleotide sequence of the T24 human bladder carcinoma oncogene and its normal homologue", <i>Nature</i> 302 1983, 33-37
	AE	Chang et al., "Comparative inhibition of ras p21 protein synthesis with phosphorus-modified antisense oligonucleotides", <i>Anti-Cancer Drug Design</i> 1989, 4, 221-232
	AF	Chang et al., "Antisense inhibition of ras p21 expression that is sensitive to a point mutation", <i>Biochemistry</i> 1991, 30, 8283-8286
	AG	Chiang et al., "Antisense Oligonucleotides Inhibit Intercellular Adhesion Molecule 1 Expression by Two Distinct Mechanisms", <i>J. Biol. Chem.</i> 1991, 266:18162-18171
	AH	De Mesmaeker et al., "Antisense Oligonucleotides", <i>Acc. Chem. Res.</i> 1995, 28:366-374
	AI	Dignam et al., "Accurate transcription initiation by RNA polymerase II in a soluble extract from Isolated mammalian nuclei", <i>Nucleic Acids Res.</i> 1983, 11, 1475-1489

EXAMINER

DATE CONSIDERED

Form PTO-1449 Modified	Docket No. ISPH-0763	Serial No. Not yet assigned
List of Patents and Publications Cited by Applicant (Use several sheets if necessary)	Applicant Monia et al.	
U.S. Department of Commerce Patent and Trademark Office	Filing Date Herewith	Group Not yet assigned

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

AJ	Feramisco et al., "Transient reversion of <i>ras</i> oncogene-induced cell transformation by antibodies specific for amino acid 12 of <i>ras</i> protein", <i>Nature</i> 1985, 314, 639-642
AK	Gebeyehu, G., et al., "Novel biotinylated nucleotide analogs for labeling and colorimetric detection of DNA", <i>Nucl. Acids Res.</i> 1987, 15:4513-4534
AL	Georges, R.N. et al., "Prevention of Orthotopic Human Lung Cancer Growth by Intratracheal Instillation of a Retroviral Antisense K-ras Construct", 1993, <i>Cancer Research</i> , 53, 1743-1746.
AM	Greenberg, M.E., in <i>Current Protocols in Molecular Biology</i> , (F.M. Ausubel, R. Brent, R.E. Kingston, D.D. Moore, J.A. Smith, J.G. Seidman and K. Strahl, eds.), John Wiley and Sons, NY
AN	Hall et al., "Identification of transforming gene in two human sarcoma cell lines as a new member of the <i>ras</i> gene family located on chromosome 1", <i>Nature</i> 1983, 303: 396-400
AO	Hall and Brown, "Human N-ras: cDNA cloning and gene structure", <i>Nucleic Acids Res.</i> 1985, 13, 5255-5268
AP	Holt et al., "An Oligomer Complementary to c-myc mRNA Inhibits Proliferation of HL-60 Promyelocytic Cells and Induces Differentiation", <i>Mol. Cell Biol.</i> 1988, 8, 963-973
AQ	Kabanov et al., "A new class of antivirals: antisense oligonucleotides combined with a hydrophobic substituent effectively inhibit influenza virus reproduction and synthesis of virus-specific proteins in MDCK cells", <i>FEBS Lett.</i> 1990, 259, 327-330
AR	Kahn et al., The c-K-ras gene and human cancer (review), <i>Anticancer Res.</i> 1987, 7, 639-652

EXAMINER

DATE CONSIDERED

Form PTO-1449 Modified  List of Patents and Publications Cited by Applicant (Use several sheets if necessary)  U.S. Department of Commerce	Docket No.: TSPH-0763  Applicant Monia et al.	Serial No. Not yet assigned
	Filing Date: Herewith	Group Not yet assigned

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

AS	Kawasaki et al., "Uniformly Modified 2'-Deoxy-2'-fluoro Phosphorothioate Oligonucleotides as Nuclease-Resistant Antisense Compounds with High Affinity and Specificity for RNA Targets", <i>J. Med. Chem.</i> 1993, 36, 831-841
AT	Kingston, R.E., in <i>Current Protocols in Molecular Biology</i> , (F.M. Ausubel, R. Brent, R.E. Kingston, D.D. Moore, J.A. Smith, J.G. Seidman and K. Strahl, eds.), John Wiley and Sons, NY.
AU	Kornberg, A., <i>DNA Replication</i> , W.H. Freeman & Co., San Francisco, 1980, pp 75-77
AV	Lima et al., "Implication of RNA Structure on Antisense Oligonucleotide Hybridization Kinetics", <i>Biochemistry</i> 1992, 31, 12055-12061
AW	Letsinger et al., "Cholesteryl-conjugated oligonucleotides: Synthesis, properties, and activity as inhibitors of replication of human immunodeficiency virus in cell culture", <i>Proc. Natl. Acad. Sci. USA</i> 1989, 86, 6553-6556
AX	Mukhopadhyay, T. et al., "Specific Inhibition of K-ras Expression and Tumorigenicity of Lung Cancer Cells by Antisense RNA", (1991) <i>Cancer Research</i> 51, 1744-1748
AY	Martin, P., "Ein neuer Zugang zu 2'-O-Alkylribonucleosiden und Eigenschaften deren Oligonucleotide", <i>Helv. Chim. Acta</i> 1995, 78, 486-504
AZ	Manoharan et al., "Cholic Acid-Oligonucleotide Conjugates for Antisense Applications", <i>Bioorg. Med. Chem. Let.</i> 1994, 4, 1053-1060
BA	Manoharan et al., "Introduction of a Lipophilic Thicether Tether in the Minor Groove of Nucleic Acids for Antisense Applications", <i>Bioorg. Med. Chem. Let.</i> 1993, 3, 2765-2770

EXAMINER

DATE CONSIDERED

Form PTO-1449 Modified		Docket No. ISPH-0763	Serial No. Not yet assigned
List of Patents and Publications Cited by Applicant (Use several sheets if necessary)		Applicant Monia et al.	
U.S. Department of Commerce		Filing Date Herewith	Group Not yet assigned

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

BB	Manoharan et al., "Antisense Strategies", <i>Ann. N.Y. Acad. Sci.</i> 1992, 660, 306-309
BC	Manoharan et al., "Lipidic Nucleic Acids", <i>Tetrahedron Lett.</i> 1995, 36, 3651-3654
BD	Manoharan et al., "Oligonucleotides Conjugates: Alteration of the Pharmacokinetic Properties of Antisense Agents", <i>Nucleosides &amp; Nucleotides</i> 1995, 14, 969-973
BE	McGrath, J.P. et al., "Structure and organization of the human Ki-ras proto-oncogene and a related processed pseudogene", <i>Nature</i> 1983, 304, 501-506
BF	Nielsen et al., "Sequence-Selective Recognition of DNA by Strand Displacement with a Thymine-Substituted Polyamide", <i>Science</i> 1991, 254, 1497
BG	Oberhauser et al., "Effective incorporation of 2'-O-methyl-oligoribonucleotides into liposomes and enhanced cell association through modification with thiocholesterol", <i>Nucl. Acids Res.</i> 1992, 20, 533-538
BH	Owen et al., "Transcriptional activation of a conserved sequence element by ras requires a nuclear factor distinct from c-fos or c-jun", <i>Proc. Natl. Acad. Sci. U.S.A.</i> 1990, 87, 3866-3870
BI	Petersheim, M. and Turner, D.H., "Base Stacking and Base-Pairing Contributions to Helix Stability: Thermodynamics of Double-Helix Formation with CCGG, CCGGp, CCGGAp, ACCGGp, CCGGU <sub>p</sub> , and ACCGGU <sub>p</sub> ", <i>Biochemistry</i> 1983, 22, 256-263
BJ	Puglisi and Tinoco, "Absorbance Melting Curves of RNAs", <i>Methods in Enzymol.</i> 1989, 180, 304-325

EXAMINER

DATE CONSIDERED

Form PTO-1449 Modified	Docket No.: ISPH-0763	Serial No.: Not yet assigned
List of Patents and Publications Cited by Applicant (Use several sheets if necessary)	Applicant Monia et al.	
U.S. Department of Commerce Patent and Trademark Office	Filing Date Herewith	Group Not yet assigned

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

BK	Reddy, P.E. et al., "A point mutation is responsible for the acquisition of transforming properties by the T24 human bladder carcinoma oncogene", <i>Nature</i> 1982, 300, 149-152
BL	Sanghvi et al., "Antisense oligodeoxynucleotides: synthesis, biophysical and biological evaluation of oligodeoxynucleotides containing modified pyrimidines", <i>Nucl. Acids Res.</i> 1993, 21, 3197-3203
BM	Sanghvi, Y.S., in Crooke, S.T. and Lebleu, B., eds., <i>Antisense Research and Applications</i> , CRC Press, Boca Raton, 1993, pp. 276-288
BN	Saisou-Behmoaras, T. et al., "Short modified antisense oligonucleotides directed against Ha-ras point mutation induce selective cleavage of the mRNA and inhibit T24 cells proliferation", <i>EMBO J.</i> 1991, 10, 1111-1118
BO	Skorski, et al., "Growth Factor-dependent Inhibition of Normal Hematopoiesis by N-ras Antisense Oligodeoxynucleotides", <i>J. Exp. Med.</i> , 1992, 175, 743-750
BP	Svinarchuk et al., "Inhibition of HIV proliferation in MT-4 cells by antisense oligonucleotide conjugated to lipophilic groups", <i>Biochimie</i> 1993, 75, 49-54
BQ	Shea, "Synthesis, hybridization properties and antiviral activity of lipid-oligodeoxynucleotide conjugates", et al. <i>Nucl. Acids Res.</i> 1990, 18, 3777-3783
BR	Tidd et al., "Evaluation of N-ras oncogene anti-sense, sense and nonsense sequence methylphosphonate oligonucleotide analogues", <i>Anti-Cancer Drug Design</i> 1988, 3, 117-127
BS	Tabin, C.J. et al., "Mechanism of activation of a human oncogene", <i>Nature</i> 1982, 300, 143-149

EXAMINER

DATE CONSIDERED

Form PTO-1449 Modified		Docket No: ISPH-0763	Serial No. Not yet assigned
List of Patents and Publications Cited by Applicant (Use several sheets if necessary)		Applicant Monia et al.	
U.S. Department of Commerce Patent and Trademark Office		Filing Date Herewith	Group Not yet assigned
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)			
	BT	Taparowsky, E. et al., "Activation of the T24 bladder carcinoma transforming gene is linked to a single amino acid change", <i>Nature</i> 1982, 300, 762-765	
	BU	Taparowsky et al., "Structure and Activation of the Human N-ras Gene", <i>Cell</i> 1983 34: 581-6	
	BV	Wickstrom et al., "Human promyelocytic leukemia HL-60 cell proliferation and c-myc protein expression are inhibited by an antisense pentadecadeoxynucleotide targeted against c-myc mRNA", <i>Proc. Nat. Acad. Sci.</i> 1988, 85, 1028-1032	
EXAMINER		DATE CONSIDERED	

Form PTO-1449 Modified		Docket No. ISPH-0763	Serial No. Not yet assigned
List of Patents and Publications Cited by Applicant (Use several sheets if necessary)		Applicant Monia et al.	
U.S. Department of Commerce Patent and Trademark Office		Filing Date Herewith	Group Not yet assigned

## U. S. PATENT DOCUMENTS

Examiner		Document	Date	Name	Class	Subclass
	AA	4,871,838	10/3/89	Bos et al.	536	27
	AB	5,034,506	7/23/91	Summerton et al.	528	391
	AC	5,138,045	8/11/92	Cook et al.	536	27
	AD	5,218,105	6/8/93	Cook et al.	536	25.31
	AE	5,378,825	1/3/95	Cook et al.	536	25.34
	AF	5,459,255	10/17/95	Cook et al.	536	27.13

## FOREIGN PATENT DOCUMENTS

Examiner Initial		Document No.	Date	Country	Translation YES                    NO
	AG	WO 92/15680	9/17/92	PCT	X
	AH	PCT/US88/01024	3/22/88	PCT	X
	AI	WO 94/26764	11/24/94	PCT	X

EXAMINER	DATE CONSIDERED